promoting the biological activity of said ABC1 polypeptide and detecting a difference in said biological activity following said contacting relative to when said compound is not present

H1 (cont.)

wherein said biological activity is binding or hydrolysis of adenosine triphosphate (ATP) and wherein said human ABC1 (hABC1) comprises amino acids 1-60 of SEQ ID NO: 1,

thereby identifying an ABC1 modulating agent.

---

4 ~~143~~. (Four Times Amended) A process for identifying a compound that modulates mammalian ABC1 polypeptide biological activity comprising contacting a compound with a membrane comprising a mammalian ABC1 polypeptide <u>comprising an amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 1 and having lipid transporting activity</u>, in the presence of a lipid under conditions promoting transport of said lipid across said membrane, wherein said lipid is phospholipid or cholesterol, and detecting a difference in said transport following said contacting relative to when said compound is not present thereby identifying a mammalian ABC1 modulating agent.

H2

---

17 ~~161~~. (Three Times Amended) A process for identifying a compound that modulates ~~mammalian~~ <u>human</u> ABC1 polypeptide biological activity and is useful in modulating plasma cholesterol levels in a mammal comprising contacting a compound with a membrane comprising a human ABC1 polypeptide, wherein said polypeptide comprises amino acid residues 1-60 of SEQ ID NO: 1, and a source of one or more anions under conditions promoting transport of said one or more anions across said membrane and detecting a difference in said transport following said contacting relative to when said compound is not present thereby identifying a mammalian ABC1 modulating agent.

H3

---

21 ~~166~~. (Three Times Amended) A process for identifying a compound that modulates ~~mammalian~~ <u>human</u> ABC1 polypeptide biological activity for use in treating

H4

4

CAD comprising contacting a compound with a membrane comprising a human ABC1 polypeptide and interleukin-1 under conditions promoting transport of said interleukin-1 across said membrane and detecting a difference in said transport following said contacting relative to when said compound is not present and wherein said human ABC1 comprises amino acids 1-60 of SEQ ID NO: 1, thereby identifying a mammalian ABC1 modulating agent useful for treating CAD.

22 ~~168~~. (Twice Amended) The process of claim ~~167~~ 21 ~~166~~ wherein said human ABC1 comprises the amino acid sequence of SEQ ID NO: 1.

23 ~~169~~. (Twice Amended) A process for identifying a compound that modulates ~~mammalian~~ human ABC1 protein biological activity and is useful in modulating human plasma cholesterol levels comprising contacting a compound with a human ABC1 protein that has ABC1 biological activity and in the presence of a protein that binds to said human ABC1 protein under conditions promoting binding of said protein to said ABC1 polypeptide, wherein said human ABC1 protein comprises amino acids 1-60 of SEQ ID NO: 1, and detecting a difference in said binding following said contacting relative to when said compound is not present thereby identifying a mammalian ABC1 modulating agent.

24 ~~172~~. (Twice Amended) The process of claim ~~169~~ 23 wherein said ABC1 polypeptide is present in the membrane ~~is part~~ of an intact cell.

28 ~~176~~. (Twice Amended) A process for identifying a compound that modulates mutant human ABC1 (hABC1) polypeptide biological activity comprising contacting a compound with a mutant hABC1 polypeptide having ABC1 polypeptide biological activity, comprising from 1 to 5 amino acid differences relative to the sequence of SEQ ID NO: 1, and a member selected from the group consisting of a lipid, a protein, ATP, and interleukin-1, and detecting a difference in said biological activity following said

185

contacting relative to when said compound is not present thereby identifying a mutant hABC1 modulating agent.

29
30 ~~179~~. (Twice Amended) The process of claim ~~143~~ ~~178~~ wherein said hABC1 comprises a detectable label.

4
32 ~~181~~. (Twice Amended) The process of ~~claims~~ claim ~~143~~ wherein said ABC1 polypeptide is a recombinant polypeptide.

184. (Twice Amended) A process for identifying a compound that modulates cholesterol levels in a mammal comprising administering to said mammal an effective amount of a compound that has ABC1 modulating activity in the process of claim 143 and determining a difference in cholesterol level in said mammal following said administering thereby identifying a compound that modulates cholesterol levels in a mammal.

188. (Twice Amended) The process of claim ~~182~~ 184 wherein said mammal is a human.

33 ~~213~~. (Twice Amended) A process for identifying a compound that modulates lipid transport across a mammalian cell that includes a cell membrane that includes ABC1 polypeptide comprising an amino acid sequence with least 85% identity to the amino acid sequence of SEQ ID NO: 1 and having lipid transporting activity, comprising testing ~~a~~ said mammalian cell ~~that~~ wherein said cell includes ~~in the cell~~ a lipid selected from the group consisting ~~or~~ of phospholipid and cholesterol, under conditions promoting transport of said lipid across said membrane, and comparing transport of said lipid in the presence and absence of a test compound whereby a difference in said transport indicates modulation, thereby identifying said compound as a modulator of lipid transport.

Please add the following new claims:

46 226. (New) The process of claim 4 ~~143~~ wherein said percent identity is at least 90% identity.

47 227. (New) The process of claim 4 ~~143~~ wherein said percent identity is at least 95% identity.

48 228. (New) The process of claim 4 ~~143~~ wherein said ABC1 polypeptide comprises the amino acid sequence of SEQ ID NO: 1.

49 229. (New) The process of claim 33 ~~213~~ wherein said percent identity is at least 90% identity.

50 230. (New) The process of claim 33 ~~213~~ wherein said percent identity is at least 95% identity.

51 231. (New) The process of claim 33 ~~213~~ wherein said ABC1 polypeptide comprises the amino acid sequence of SEQ ID NO: 1.

REMARKS

Applicants respond as follows:

Application Status

187